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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT PAPER NUMBER

1624

DATE MAILED: 04/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/835,523

Applicant(s)

WU ET AL.

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 44-47 is/are pending in the application.
- 4a) Of the above claim(s) 44-47 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1, 3, 4, 21, 23, 24, and 34 is/are allowed.
- 6) ☒ Claim(s) 2, 5-12, 14-20, 22, 25-32 and 35-40 is/are rejected.
- 7) ☒ Claim(s) 13 and 33 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment of 01-24-03 has been considered. The amended claims 1, 4, 7, 10, 11, and 14, and cancellation of claims 41-43 have overcome the previous 112/2nd paragraph issues. However, said amended claims have not overcome the rejections of 102 (b) and (e) based on **Kobayashi et. al.** (EP'484), and **Delaszlo** (US'163) for reasons set forth below. Therefore, the rejections of 102 and 103 remain outstanding while the rejection of 112/2nd is withdrawn herein.

Newly submitted claims 44-47 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Said claims are drawn to "a method of making a pharmaceutical composition" which requires a search beyond the scope of the original claims, and thus, poses a burden of searching.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 44-47 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

The amendment to the specification cannot be entered because it does not refer to the page and line number of the instant disclosure. Thus, it is confusing as to what need to be added or deleted, and where.

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The specification was objected to because on pages 57-61, they list compounds' names with "...pyrazinecarboxylate". In particular, these are compounds on lines 3-9 of page 57, and on line 11 of page 59; also on line 11 of page 61. Furthermore, it has just been noted that on page 57, compounds on lines 15-19 are named with "piperazine", which is also inconsistent with the claimed formulae. Applicant is advised to make correction for said compounds' names in the instant disclosure, and not in the pregrant publication of U.S. 2002/0028814-A1.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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1. Claim 31 remains rejected under 35 U.S.C. 102(b) as being anticipated by **Kobayashi et. al.** (EP 104,484).

The rejection is maintained for the reason stated previously, and for the following reason:

Applicant asserted that claim 31 could not be ^{anticipated} ~~asserted~~ by **Kobayashi et. al.** because the compound of Kobayashi et. al. has an ester group on the phenyl, whereas the claimed compound does not. However, in claim 31, R^2 can be an aryl group substituted with R^3 as a **carboxy**. Claim 31 also allows for “**ester thereof**” with no specific indication where the ester can be. Thus, it would be reasonable to interpret that the “carboxy” (of R^3) on the aryl group (of R^2) could also have the form “ester”. Thus, anticipation stands.

Note, because Kobayashi apply their compounds in killing weeds, the composition of claim 34 is not anticipated by said teaching.

2. Claims 11 and 14 remain rejected under 35 U.S.C. 102(e) as being anticipated by **Delaszlo** (US'163).

The rejection is maintained for the reason stated previously, and for one below:

Although said claims have been amended to eliminate the “*carboxy*” group from the definition of R^3 . Said deletion has not overcome the teaching of **Delaszlo** because the disclosed compounds read on the claimed compound when R^3 represents **C₁-C₉ alkyl substituted with carboxy**. Thus, because the “carboxy” group has **not** been deleted from the list of substituents on R^3 , the disclosed compounds still anticipate compounds recited in claims 11 and 14.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 7-10, 17-20, 27-30, and 37-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being **enabling for the method of treating Parkinson's disease**, does **not** reasonably provide enablement for the method of treating Alzheimer's disease, Huntington's disease, and other neuronal activity (e.g., promoting neuronal regeneration, preventing neurodegeneration, etc.). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 7, 17, 27, and 37 recite a "method of effecting a neuronal activity" which encompasses both "inhibiting" and "promoting" a neuronal activity. The specification provides bioassay for the inhibition of "rotamase", and effect on dopaminergic neuron. Because the specification does not provide a correlation between the inhibition of "rotamase" with neuronal activity, one cannot draw a conclusion whether or not the claimed compounds can promote neuronal regeneration, or prevent neurodegeneration. Currently, there is no known agent that can regenerate a neuron, nor is there one for preventing neurodegeneration. Regarding Alzheimer's disease, it has been known to be associated with the formation of amyloids, which has no known cause. The present treatment for Alzheimer's disease is a cholinesterase inhibitor

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(e.g. TACRINE^(R)), and that only delays the progression of the disease. Regarding Huntington's disease, there is also no known cause, and the currently, antipsychotic agent is used to alleviate symptoms. Thus, with a demonstration on dopaminergic neuron, the claimed compounds at best can only treat Parkinson's disease. One skilled in the art will have to carry out undue experimentation to extend the use of the claimed compounds for the treatment of Alzheimer's disease, Huntington's disease as well as promoting neuronal regeneration, or preventing neurodegeneration.

4. Claims 5, 6, 15, 16, 35, and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Said claims recite a "pharmaceutical composition further comprising an additional neurotrophic factor". The specification does not describe how such a neurotrophic factor can be incorporated with the claimed compound in the same pharmaceutical composition. First of all, said factor appear to be a protein, which can be metabolized in the gastrointestinal tract, and liver, and thus will lose efficacy. Thus, such a combination is not a simple addition, and requires undue experimentation in terms of pharmacokinetics, and adverse reactions.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 2, 12, 22, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reason apply:

- a. Claim 2 appears to claim the same compounds as claim 1 since the preamble “non-immunosuppressive does not result in a structural change.
- b. Claim 12 appears to claim the same compounds as claim 11 since the preamble “non-immunosuppressive does not result in a structural change.
- c. Claim 22 appears to claim the same compounds as claim 21 since the preamble “non-immunosuppressive does not result in a structural change.
- d. Claim 32 appears to claim the same compounds as claim 31 since the preamble “non-immunosuppressive does not result in a structural change.

Claim Objections

6. Claims 13 and 33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

7. Claims 1, 3, 4, 21, 23, 24, and 34 are allowed since the prior arts of record do not teach or suggest compounds of formulae I, III, and pharmaceutical composition thereof.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:30-5:00) & every Saturday morning (starting from 4-7-03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Tamthom N. Truong
Examiner
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April 12, 2003